American ALS patient database, launched about two years ago, promises to provide new outcome data that should further raise the standard of care.

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Status Epilepticus

STATUS EPILEPTICUS IS characterized by abnormally prolonged seizure activity. Although there are numerous forms of status epilepticus that parallel, in part, the various types of isolated seizures, this epitome is directed toward generalized convulsive status epilepticus (GCSE) in adults and older children. GCSE includes the most common forms of status epilepticus (generalized, tonic-clonic, and myoclonic) and is associated with relatively high levels of morbidity and mortality. Because a variety of studies suggest that the typical, isolated tonic-clonic seizure in adults lasts no more that 3 to 4 minutes, an operational definition can emphasize the time at which therapy for status epilepticus should be initiated. GCSE can be defined as at least *five* minutes of either continuous seizures or two or more discrete seizures between which there is incomplete consciousness recovery. This definition does not refer to a mechanism that defines the transition from an isolated seizure to status epilepticus. Recent experimental observations, however, indicate that potentially important molecular "switches" occur in neurotransmitter receptors within this general time frame and may have a critical role in causing the enhanced neuronal excitability that characterizes status epilepticus.

A comprehensive, community-based prospective study of status epilepticus from Richmond, Virginia, suggests that the frequency of cases of status epilepticus in the US is approximately 100,000 to 150,000 per year, roughly twice as high as previously thought. This study has also verified a number of previous conclusions regarding the prime importance of etiology and age as determinants of outcome in status epilepticus. Patients with GCSE from etiologies having a chronic or remote basis (such as refractory epilepsy, discontinuation of antiepileptic drugs, or chronic ethanol abuse) generally respond well to treatment and recover. In contrast, patients with GCSE induced by more acute processes (such as metabolic abnormalities, infection, stroke, head trauma, or drug toxicity) often have seizures that are resistant to typical, front-line therapy and are associated with a substantially higher morbidity and mortality. Also, patients older than 60 are significantly more prone to complications related to GCSE.

Two recent advances have been made in the initial treatment of patients with GCSE. Intravenous lorazepam has supplanted intravenous diazepam as the most commonly used first-line drug therapy. Although lorazepam and diazepam have similar efficacy in aborting GCSE, the preference for lorazepam stems from the recognition that it has a significantly longer duration of antiseizure effect (12 to 24 hours for lorazepam compared to 15 to 30 minutes for diazepam). The other new aspect of initial therapy concerns the recent availability of fosphenytoin (Cerebyx). Fosphenytoin is a water-soluble pro-drug of phenytoin that is converted to phenytoin by nonspecific phosphatases. The water-solubility allows fosphenytoin to be combined with any intravenous fluid (as opposed to phenytoin, which precipitates when mixed with glucose-containing solutions). Fosphenytoin can also be infused faster (150 mg per minute of phenytoin equivalents) than phenytoin (50 mg per minute). The time to reach therapeutic serum levels of phenytoin is approximately the same for both drugs when using the suggested infusion rates. Theoretically, the lack of propylene glycol as a diluent for fosphenytoin suggests there should be fewer hypotensive or adverse cardiac effects compared to intravenous phenytoin. Other than a lower rate of infusion site reactions with fosphenytoin, however, no differences between the two drugs in frequency or scope of adverse events have been shown thus far.

Refractory status epilepticus refers to a situation in which patients do not respond to front-line therapy with lorazepam and phenytoin (or fosphenytoin) followed by loading doses of phenobarbital. Patients with refractory status epilepticus usually need to be managed in an intensive care unit, and they require careful neurological assessment, including regular monitoring with electroencephalography. Until recently, barbiturate coma was the preferred treatment for refractory status epilepticus, despite the recognition that this form of therapy was associated with a high frequency of complications, most notably hypotension. Intravenous midazolam and propofol have recently become popular alternatives to phenobarbital; these drugs appear to have a substantially lower incidence of complications.

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